REMARKS

Claims 33-36 and 45 were pending in the application. Claims 36 and 45 have been cancelled, claims 33 and 35 have been amended, and claims 46-56 have been added. Accordingly, following entry of the amendments presented herein, claims 33-35 and 46-56 will be pending. For the Examiner's convenience, a copy of the claims as they will be pending upon entry of the present amendment, is set forth herein as Appendix A.

Attached hereto is a marked-up version of the changes made to the claims by the current amendments. The attached page is captioned "Version With Markings to Show Changes Made".

Support for the amendments to the claims as well as the new claims can be found throughout the specification and in the claims as originally filed. Specifically, support for the recitation of SEQ ID NO:2 in claim 33 can be found at least at page 11, lines 29-30. Support for the recitation of "a portion thereof" in claim 33 can be found at least at page 4, lines 31-33. Support for the recitation of percent homology in new claims 46-50 can be found at least at page 11, line 38 to page 12, line 4. Support for the recitation of "wherein the protein interacts with a Rel Homology domain of an NF-AT family protein" in new claims 46-50 can be found at least at page 9, line 39 to page 10, line 1. Support for new claims 51-56 can be found at least at page 21, lines 26-38 of the instant specification.

No new matter has been added. The foregoing claim amendments and cancellations should in no way be construed as an acquiescence to any of the Examiner's rejections, and have been made solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Present Invention is Free of Prior Art

The Applicants gratefully acknowledge the Examiner's position that "[t]he instant NIP45-specific antibodies, wherein NIP45 is set forth in SEQ 1D NOs: 1 and 2 appears free of the prior art."

B

Objections to the Specification

1. Amendments to the Specification

The Examiner states that the specification must be amended to indicate appropriate SEQ ID NOs.

Accordingly, Applicants have amended the specification to insert appropriate SEQ ID NOs at the paragraph beginning on page 5, line 32, thereby rendering the instant objection moot.

2. Priority

The Examiner states that "[i]f applicant desires priority under 35 § U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application."

Accordingly, Applicants have amended the specification to insert a specific reference to the earlier filed applications to which the instant application claims priority under 35 U.S.C. § 120, thereby rendering the instant objection moot.

3. Availability of References Cited in the Information Disclosure Statement

The Examiner states that the references cited in the Applicants' IDS (Paper No. 3) were unavailable to the Examiner.

Accordingly, for the Examiner's convenience, Applicants are submitting herewith copies of all references cited in Paper No. 3.

4. Title of the Invention

The Examiner states that the "title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention."

Applicants have amended the title to "*ANTIBODIES FOR NF-AT INTERACTING PROTEIN, NIP45, AND METHODS OF USE THEREFOR*", thereby rendering the instant objection moot.

5. Formal Drawings

The Examiner states that the submitted drawings do not comply with the requirements of 37 CFR 1.84.

Applicants respectfully submit that formal drawings pursuant to 37 CFR 1.84 will be filed upon allowance.

6. Informalities

The Examiner states that the "application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected."

Applicants have reviewed the application and have amended the specification to correct errors and omissions, thereby rending this objection moot. Applicants note that no trademarks without the proper identifying nomenclature were found in the instant specification.

Accordingly, Applicants respectfully request withdrawal of the objections to the specification.

Rejection of Claims 33-36 Under 35 U.S.C. § 112, first paragraph

Claims 33-36 were rejected under 35 U.S.C. §112, first paragraph, on the grounds that the "specification does not provide adequate written description of the claimed invention, namely, 'NIP45 protein', other than that set forth in SEQ ID NO:2 or encoded by SEQ ID NO:1." Claims 33-36 were further rejected under 35 U.S.C. § 112, first paragraph, on the grounds that "the specification, while being enabling for "NIP45 protein" set forth in SEQ ID NO:2 or encoded by SEQ ID NO:1, does not reasonably provide enablement for any 'NIP45 protein' as the claimed antibody specificity."

Applicants respectfully traverse this rejection. However, in the interest of expediting prosecution, Applicants have amended the claims to recite an antibody that specifically binds to a protein comprising the amino acid sequence set forth in SEQ ID NO:2, or a portion thereof (claim 33). New claims 46-50 have been added to recite antibodies which bind to a protein comprising an amino acid sequence at least 60 %, 70%, 80%, 90% and 95% homologous to the

amino acid sequence of SEQ ID NO: 2, respectively, wherein the protein interacts with a Rel Homology domain of an NF-AT family protein.

Furthermore, Applicants submit that contrary to the Examiner's assertion, the term "NIP45 protein" is sufficiently described in the instant specification to enable the ordinarily skilled artisan to produce antibodies that specifically bind NIP45 protein. In particular, Applicants provide the nucleotide (SEQ ID NO:1) and amino acid sequence (SEQ ID NO:2) of a NIP45 protein. In addition, Applicants state at least at page 11, lines 6-14 of the instant specification that "nucleic acid molecules encoding NIP45 proteins from other species, and thus which have a nucleotide sequence that differs from the mouse sequence of SEQ ID NO: 1 but that is related to the mouse sequence, are intended to be within the scope of the invention." Thus, NIP45 proteins corresponding to natural allelic variants, human, and other mammalian homologues of the mouse NIP45 can be isolated based on their homology SEQ ID NO:1 or SEQ ID NO:2 using standard hybridization techniques under stringent hybridization conditions.

Applicants also teach the functional characteristics that correlate to the structural characteristics of NIP45 proteins. For example, Applicants teach at least at page 7, lines 2-4 and Example 6 of the instant specification that "NIP45 synergizes with NF-AT to stimulate transcription from promoters containing NF-AT binding sites and, moreover, synergizes with NF-AT and c-Maf to stimulate transcription from the IL-4 promoter (see Example 6)." Applicants further teach methods of detecting the ability of the claimed NIP45 proteins to interact with NF-AT, *e.g.*, through standard *in vitro* interaction assays using a glutathione-S-transferase (GST)-NF-AT RHD fusion protein (page 10, lines 2-8 of the instant specification).

In summary, Applicants submit that that based on the disclosed structural and functional features of the NIP45 proteins, the correlation between the structural and functional features of the NIP45 proteins, and the art-recognized methods of producing and detecting NIP45 proteins, it would have been routine for the ordinarily skilled artisan to produce homologues of the disclosed NIP45 proteins. Thus, the recitation of the term "NIP45 protein" in the claims is sufficiently described and enabled by the instant specification.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 33-36 under 35 U.S.C. § 112, first paragraph.

Rejection of Claim 36 Under 35 U.S.C. § 112, first paragraph

Claim 36 was rejected under 35 U.S.C. § 112, first paragraph, on the grounds that undue experimentation would be required to practice the claimed methods due to a lack of established clinical protocols in the art for effective pharmaceutical compositions comprising antibodies to target intracellular targets.

Applicants respectfully traverse. However, in the interest of expediting prosecution, Applicants have cancelled claim 36 thereby rendering the instant rejection moot. Applicants reserve the right to pursue claim 36 as originally filed in this or a separate application(s).

Rejection of Claims 33-36 Under 35 U.S.C.§ 112, second paragraph

Claims 33-36 were rejected under 35 U.S.C.§ 112, second paragraph, on the grounds that the recitation of "NIP45 protein" only describes the antibody specificity of interest by an arbitrary protein name. Claim 35 was rejected on the grounds that it "lacks proper antecedent basis to the antibody of claim 33, given that claim 35 is conjugated or labeled antibody and claim 33 is not a conjugated or labeled antibody."

Applicants respectfully traverse and request reconsideration.

As set forth above, the term "NIP45 protein" is described in the instant specification as referring to a protein with particular structural and functional characteristics based on which, an ordinarily skilled artisan could produce a number of NIP45 homologues. Furthermore, Applicants have amended the claims to specifically recite the SEQ ID NO of the NIP45 protein thereby obviating the rejection that the claims only describe the claimed antibody specificity "by an arbitrary protein name."

With respect to the rejection of claim 35 for improper antecedent basis, Applicants have amended claim 35 such that it is directed to the antibody of claim 34, "wherein the antibody is further coupled to a detectable substance." Claim 35 thus has proper antecedent basis to the antibody of claim 33, thereby obviating the instant rejection.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the instant rejection of claims 33-36 under 35 U.S.C. § 112, second paragraph.

B

CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP

Cynthia L. Kanik, Ph.D.
Reg. No. 37,320
Attorney for Applicants

28 State Street
Boston, MA 02109
Tel. (617) 227-7400

Dated: **March 4, 2002**

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The title was replaced by the following:

-- ANTIBODIES FOR NF-AT INTERACTING PROTEIN, NIP45, AND METHODS OF USE THEREFOR--

The paragraph beginning at page 1, line 10, was replaced with the following:

--**Related Applications**

This application is a divisional application of U.S. Serial No. 09/192,611, filed November 16, 1998 (now U.S. Patent No. 6,090,561) which is a divisional application of U.S. Serial No. 08/755,584, filed November 25, 1996 (now U.S. Patent No. 5,858,711), the entire contents of which are expressly incorporated herein by reference.—

The paragraph beginning on page 5, line 32 was replaced with the following:

--Figure 4 depicts the nucleotide (SEQ ID NO:1) and predicted amino acid sequences (SEQ ID NO:2) of the original NIP45 cDNA isolate.--

The paragraph beginning on page 30, line 24 was replaced with the following:

-- Yet another aspect of the invention pertains to methods of modulating NIP45 activity in a cell. The modulatory methods of the invention involve contacting the cell with an agent that modulates NIP45 activity such that NIP45 activity in the cell is modulated. The agent may act by modulating the activity of NIP45 protein in the cell or by modulating transcription of the NIP45 gene or translation of the NIP45 mRNA. As used herein, the term "modulating" is intended to include inhibiting or decreasing NIP45 activity and stimulating or increasing NIP45 activity. Accordingly, in one embodiment, the agent inhibits NIP45 activity. An inhibitory

agent may function, for example, by directly inhibiting NIP45 activity or by inhibiting an interaction between NF-AT and NIP45. In another embodiment, the agent stimulates NIP45 activity. A stimulatory agent may function, for example, by directly stimulating NIP45 activity or by promoting an interaction between NF-AT and NIP45. Methods for modulating NIP45 activity are described further in U.S. Serial No. 08/755,592, entitled "*Methods for Regulating T cell Subsets by Modulating Transcription Factor Activity*", filed on November 25, 1996 ~~(Attorney Docket No. HUI-021CP)~~, the entire contents of which are expressly incorporated herein by reference.--

In the Claims:

Claims 36 and 45 were cancelled

Claims 33 and 35 were amended as follows:

33. **(Amended)** An antibody that specifically binds ~~NIP45 protein~~ to a protein comprising the amino acid sequence set forth in SEQ ID NO:2, or a portion thereof.

35. **(Amended)** The antibody of claim 34, ~~which is~~ wherein the antibody is further coupled to a detectable substance.

Claims 46-56 were added as follows:

46. **(New)** An antibody that binds to a protein comprising an amino acid sequence at least 60 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

47. **(New)** The antibody of claim 46, wherein the antibody binds to a protein comprising an amino acid sequence at least 70 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

48. **(New)** The antibody of claim 46, wherein the antibody binds to a protein comprising an amino acid sequence at least 80 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

49. **(New)** The antibody of claim 46, wherein the antibody binds to a protein comprising an amino acid sequence at least 90 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

50. **(New)** The antibody of claim 46, wherein the antibody binds to a protein comprising an amino acid sequence at least 95 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

51. **(New)** An antibody that binds to an antigenic peptide comprising at least 8 amino acid residues of the amino acid sequence set forth in SEQ ID NO: 2, such that the antibody forms a specific immune complex with a protein that interacts with a Rel Homology domain of an NF-AT protein.

52. **(New)** The antibody of claim 51, wherein the peptide comprises at least 10 amino acid residues of the amino acid sequence set forth in SEQ ID NO:2.

53. **(New)** The antibody of claim 51, wherein the peptide comprises at least 15 amino acid residues of the amino acid sequence set forth in SEQ ID NO:2.

54. **(New)** The antibody of claim 51, wherein the peptide comprises at least 20 amino acid residues of the amino acid sequence set forth in SEQ ID NO:2.

55. **(New)** The antibody of claim 51, wherein the peptide comprises at least 30 amino acid residues of the amino acid sequence set forth in SEQ ID NO:2.

56. **(New)** The antibody of claim 51, wherein the peptide is hydrophilic.

APPENDIX A

Pending Claims

33. An antibody that specifically binds to a protein comprising the amino acid sequence set forth in SEQ ID NO:2, or a portion thereof.

34. The antibody of claim 33, which is a monoclonal antibody.

35. The antibody of claim 34, wherein the antibody is further coupled to a detectable substance.

46. An antibody that binds to a protein comprising an amino acid sequence at least 60 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

47. The antibody of claim 46, wherein the antibody binds to a protein comprising an amino acid sequence at least 70 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

48. The antibody of claim 46, wherein the antibody binds to a protein comprising an amino acid sequence at least 80 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

49. The antibody of claim 46, wherein the antibody binds to a protein comprising an amino acid sequence at least 90 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

50. The antibody of claim 46, wherein the antibody binds to a protein comprising an amino acid sequence at least 95 % homologous to the amino acid sequence set forth in SEQ ID NO: 2, wherein the protein interacts with Rel Homology domain of an NFAT family protein.

51. An antibody that binds to an antigenic peptide comprising at least 8 amino acid residues of the amino acid sequence set forth in SEQ ID NO: 2, such that the antibody forms a

specific immune complex with a protein that interacts with a Rel Homology domain of an NF-AT protein.

52. The antibody of claim 51, wherein the peptide comprises at least 10 amino acid residues of the amino acid sequence set forth in SEQ ID NO:2.

53. The antibody of claim 51, wherein the peptide comprises at least 15 amino acid residues of the amino acid sequence set forth in SEQ ID NO:2.

54. The antibody of claim 51, wherein the peptide comprises at least 20 amino acid residues of the amino acid sequence set forth in SEQ ID NO:2.

55. The antibody of claim 51, wherein the peptide comprises at least 30 amino acid residues of the amino acid sequence set forth in SEQ ID NO:2.

56. The antibody of claim 51, wherein the peptide is hydrophilic.